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APPLICATION NO. FIRST NAMED INVENTOR ATTORNEY DOCKET NO. CONFIRMATION NO. FILING DATE 09/778,672 02/07/2001 Hsu Ching-Hsaing 12774-002001 4367 26161 7590 02/08/2005 **EXAMINER** FISH & RICHARDSON PC LI, QIAN JANICE 225 FRANKLIN ST **ART UNIT** PAPER NUMBER BOSTON, MA 02110 1632

DATE MAILED: 02/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

## Advisory Action Before the Filing of an Appeal Brief

Application No.	Applicant(s)		
09/778,672	CHING-HSAING ET AL.		
Examiner	Art Unit		
Q. Janice Li	1632		

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The MAILING DATE of this communication appe	ars on the cover sheet with the o	correspondence add	ress
THE REPLY FILED 22 December 2004 FAILS TO PLACE THIS	S APPLICATION IN CONDITION F	OR ALLOWANCE.	
<ol> <li>The reply was filed after a final rejection, but prior to filing must timely file one of the following replies: (1) an amend condition for allowance; (2) a Notice of Appeal (with appe Examination (RCE) in compliance with 37 CFR 1.114. The</li> <li>The period for reply expires 3 months from the mailing date</li> </ol>	ment, affidavit, or other evidence, v al fee) in compliance with 37 CFR e reply must be filed within one of t	which places the appli 41.31; or (3) a Reque	ication in st for Continued
b) The period for reply expires on: (1) the mailing date of this A no event, however, will the statutory period for reply expire Is Examiner Note: If box 1 is checked, check either box (a) or (TWO MONTHS OF THE FINAL REJECTION. See MPEP 76	ater than SIX MONTHS from the mailin (b). ONLY CHECK BOX (b) WHEN THE	g date of the final rejection	on.
Extensions of time may be obtained under 37 CFR 1.136(a). The date have been filed is the date for purposes of determining the period of exunder 37 CFR 1.17(a) is calculated from: (1) the expiration date of the set forth in (b) above, if checked. Any reply received by the Office later may reduce any earned patent term adjustment. See 37 CFR 1.704(b) NOTICE OF APPEAL	on which the petition under 37 CFR 1.1 tension and the corresponding amount shortened statutory period for reply origon than three months after the mailing da	of the fee. The appropri inally set in the final Office.	iate extension fee ce action; or (2) as
<ol> <li>The reply was filed after the date of filing a Notice of Apperwas filed on A brief in compliance with 37 CFR 41 Appeal (37 CFR 41.37(a)), or any extension thereof (37 Chas been filed, any reply must be filed within the time period.</li> </ol>	1.37 must be filed within two month FR 41.37(e)), to avoid dismissal of	is of the date of filing t	the Notice of
3. The proposed amendment(s) filed after a final rejection, (a) They raise new issues that would require further col(b) They raise the issue of new matter (see NOTE belo (c) They are not deemed to place the application in bet appeal; and/or	nsideration and/or search (see NO w); ter form for appeal by materially re	TE below);	
(d) They present additional claims without canceling a NOTE: (See 37 CFR 1.116 and 41.33(a)).			(DTO) 00 ()
<ul> <li>4.  The amendments are not in compliance with 37 CFR 1.1.</li> <li>5.  Applicant's reply has overcome the following rejection(s)</li> <li>6.  Newly proposed or amended claim(s) would be all</li> </ul>	<u>:</u> .		
non-allowable claim(s).  7. For purposes of appeal, the proposed amendment(s): a) how the new or amended claims would be rejected is provided the status of the claim(s) is (or will be) as follows:  Claim(s) allowed:  Claim(s) objected to:  Claim(s) rejected:  Claim(s) withdrawn from consideration:  AFFIDAVIT OR OTHER EVIDENCE	☐ will not be entered, or b) ☐ wivided below or appended.	II be entered and an e	explanation of
<ol> <li>The affidavit or other evidence filed after a final action, bu because applicant failed to provide a showing of good and was not earlier presented. See 37 CFR 1.116(e).</li> </ol>	t before or on the date of filing a No d sufficient reasons why the affiday	otice of Appeal will <u>no</u> vit or other evidence is	t be entered s necessary and
<ol> <li>The affidavit or other evidence filed after the date of filing entered because the affidavit or other evidence failed to o showing a good and sufficient reasons why it is necessary</li> </ol>	vercome all rejections under appea	al and/or appellant fai	Is to provide a
10. ☐ The affidavit or other evidence is entered. An explanation REQUEST FOR RECONSIDERATION/OTHER		•	
<ol> <li>The request for reconsideration has been considered bu see attachment.</li> </ol>			nce because:
12. Note the attached Information Disclosure Statement(s). (13. Other:	(PTO/SB/08 or PTO-1449) Paper N	No(s).	
		Q. Janice Li Primary Examiner	>

Art Unit: 1632

## Continuation of box 11:

Claims 24-33, 35-39, and 41-49 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Hsu et al (US 5,958,891) and Janeway Jr. (Immunobiology, 1999), in view of Pouwels et al (Intl J Food Microbial 1998;41:155-67) and Medaglini et al (PNAS 1995;92:6868-72, IDS/AI), for reasons of record and following.

Applicants first presented arguments to a previous office action (12/17/03), not the final action, asserting the prokaryotic expression system and eukaryotic expression system are not functionally equivalent in presenting antigen because the former presented the antigen to CD8+ T cells, and the later presented the antigen to CD4+ T cells, and citing '891 patent as supporting evidence.

In response, the Declaration has been addressed previously in the Office action dated 12/17/03, and applicants are reminded that the rejection has been modified since the Declaration was filed. Point 8 of the Declaration asserted that the proteins translated WITHIN the prokaryotic cells are not displayed on MHC I. However, it is noteworthy that Pouwels et al teach when using the lactobacilli for expressing foreign antigens, the production of antigens by the bacteria can occur in three different ways: intracellularly, extracellularly, and surface-bound (§ 7). Apparently, the antigen production by a prokaryotic cell is not limited to translation within said cell, and Medaglini et al have shown that engineered oral commensal bacterium could express a recombinant antigenic protein on its surface, and thus could be effectively used as a vaccine carrier for variety of antigens.

The cited paragraph of the '891 patent in the Remark is under the section of "Background of the invention", and discusses the general knowledge and theory known in the art at the time concerning mechanisms of the immune regulation in allergy, particularly the IgE-mediated allergic response, they are not specific to either the prokaryotic expression system or eukaryotic expression system.

Applicants then argue that they have shown unexpected advantage of the claimed method by a showing that the claimed method achieved more than 80% inhibition of allergen-specific IgE production and did not cause any significant change in antigen-specific IgG production contrary to the Examiner's position.

In response, the Office never intends to speculate the mechanism concerning how the claimed invention functions, this has been set forth previously. The cited Office action dated 12/17/03 or 9/22/04 are responses to applicants' argument that enhancing IgG production teaches away from the suppression of IgE production. The Examiner responded by citing the teaching of Janeway, Jr., and stated the fact that they are not conflicting because Janeway Jr. teaches shifting antibody response from IgE domination to IgG DOMINATION. Indeed, figure 1 of the specification shows an IgG domination in the recombinant bacteria treated group, no matter what the underlying mechanism is.

Concerning the 80% inhibition, it is noted in figure 8 of the '891 patent, the pCMV-Der p5 also causes a more than 80% inhibition of IgE production, thus, the degree of IgE suppression seen in the instant disclosure does not appear to be unexpected. Further, the court has determined the arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant. MPEP 716.01(c).

Applicants then pointed to fig 12.2 of Janeway, asserting the increased production of allergen-specific IgG leads to hypersensitivity and tissue damage, and thus undesired.

In response, it is noted fig 12.2 of Janeway teaches different types of hypersensitivity reaction mediated by different mechanisms. The IgGs shown in the figure differ from the IgG in the instantly disclosed IgE-mediated allergic response in the type of antigen it responds to, the effector mechanism, and the type of consequential clinical hypersensitivity reaction.

Accordingly, for reasons of record and set forth above, the rejection stands.